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(54) Colostrum protein preparation for administration to bovines

(57) Preparation for the treatment of failure of passive immunity transfer, and for supplementation of the diet, in bovines comprises a protein preparation obtained from bovine colostrum, which includes immunoglobulins and non-specific proteins, from which casein and fat have been removed.

colostrum + lactoferrin
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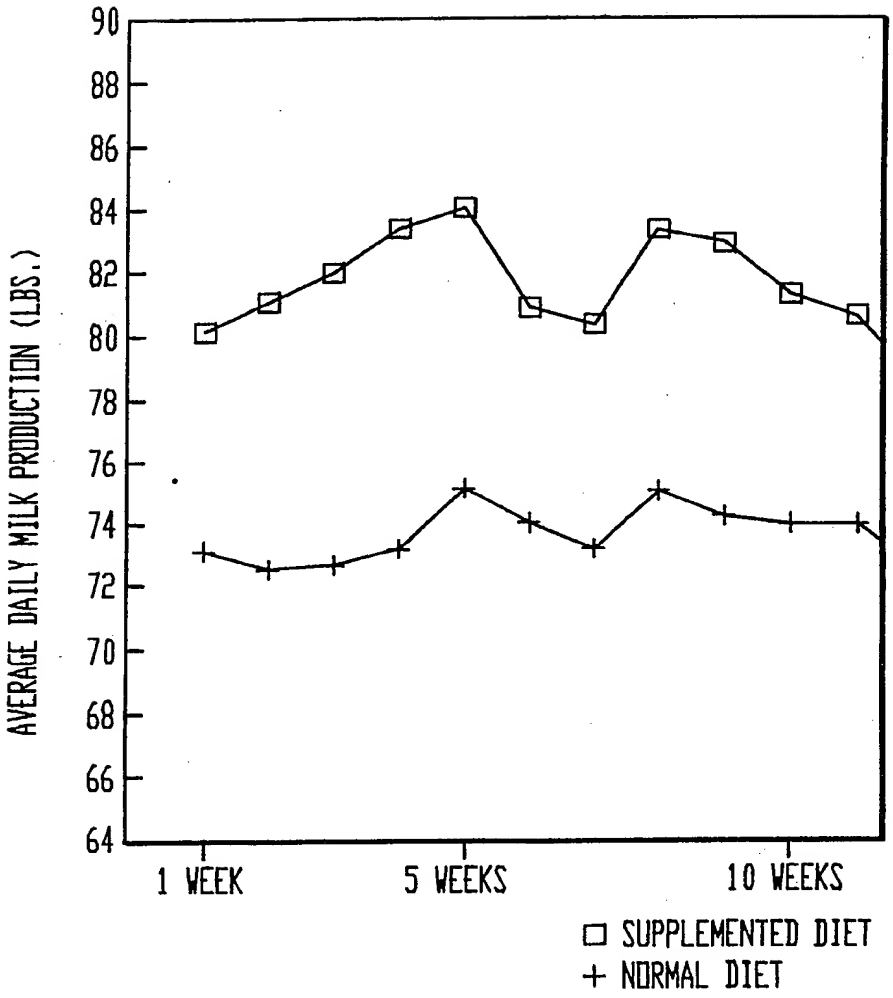
AVERAGE DAILY MILK PRODUCTION (LBS.)
90
88
86
84
82
80
78
76
74
72
70
68
66
64
1 WEEK
5 WEEKS
10 WEEKS
SUPPLEMENTED DIET
NORMAL DIET

FIG. 1

TITLE: USE OF PROTEINS FROM BOVINE COLOSTRUM TO TREAT FAILURE OF PASSIVE TRANSFER, TO PROMOTE GROWTH AND TO IMPROVE MILK PRODUCTION IN BOVINE SPECIES

BACKGROUND OF THE INVENTION

Bovine colostrum is a unique secretion of the mammary gland which is produced during the first few days of lactation. This secretion differs a great deal from normal milk. All of its components are not known, however it has been recognized to be very rich in immunoglobulins for the newborn. Intake of colostrum is essential during the first 24 hours of a calf's life. Due to the structure of the bovine placenta, transplacental transfer of immunoglobulins which confers passive immunity in most mammals is negligible. In this species nearly all passive transfer occurs by way of colostrum which is absorbed by the calf. The immunological components of colostrum include specific immunoglobulins IgG, IgM, IgA which convey passive immunity to the newborn. Peak serum immunoglobulin levels in colostrum are normally reached between 12 and 24 hours after birth. The calves intestinal permeability to these proteins is generally highest immediately after birth and declines after about six hours.

After this "window of opportunity" there is gut closure and further immunoglobulin absorption through the gut becomes negligible. Consequently calves over twenty-four hours old are essentially incapable of absorbing necessary immunoglobulins for passive transfer of immunity. This difficulty is termed failure of passive transfer (FPT) and is characterized by insufficient numbers of

immunoglobulins present in the bloodstream prior to gut closure.

This failure prevents the protection of the newborn from most pathogens encountered until the animal's own immune system is exposed to various disease antigens and produces its own immunoglobulins to these diseases.

While the role of colostrum in conferring passive immunity during the critical first hours of a neonate's life has long been appreciated, virtually no recognition to date has been made of colostrum's potential benefits after gut closure.

Consequently, methods of assisting the health of calves over 24 hours old or even adults have concentrated on purified traditional milk and conventional thinking has been the colostrum would serve no useful purpose after gut closure. As a result purified traditional milk and other methods such as administration of the highly controversial bovine growth hormone have been explored. While bovine growth hormone, when administered, has been shown to increase milk production, milk quality has suffered. There is also a psychological problem in that many consumers refuse milk from so treated dairy cows.

Still other methods have included use of genetic markers to improve overall health and performance of cows. Thus a particular genotype may be screened for aid in selection of dairy cows which possess underlying genetic criteria which will result in a desirable phenotype.

Despite all of these developments, many expensive and involving controversial technology, no one to date has recognized the potential use of all-

natural colostrum for improvement of calf and adult cow health and performance by consistent and regular dosing after gut closure.

While the presence and necessity of specific immunoglobulins in colostrum has long been appreciated, little or no attention to date has been paid to the plethora of additional non specific proteins found in colostrum. Current research has shown that colostrum contains several nonspecific proteins, for example transferin and lactoferin which bind iron, an essential growth factor for most aerobic bacteria. Enzymes such as lysozyme, xanthine oxidase and lactoperoxidase, which have been shown to have antimicrobial activity, particularly in the gut are present. Insulin-like growth promoting factors which increase uptake of glucose and amino acids by cells in the body, are present. Further, colostrum contains several additional components like conglutinin and the basic proteins β-lysin and ubiquitin, although scientific knowledge of the function of those is limited. These important characteristics of colostrum, it has now been discovered, can be used in treatments after gut closure.

Thus it is an object of the present invention to make use of colostrum as an aid to improve overall health and performance of calves and cows, particularly after gut closure.

It is yet another object of the present invention to prepare a purified injectable product derived from colostrum which includes these proteins and is useful after infancy, recognizing the continuing benefits of these proteins in even adult cows.

Further there exists a great need for a method of treating failure of passive immunity after gut closure and an object of the invention is to provide a treatment of FPT by injection of purified colostrum immunoglobulins and nonspecific proteins directly into the calf, with a high efficacy.

Another object of the invention is to provide a method of improving weight gain by calves by use of a dietary supplement of proteins derived from colostrum.

Yet another objective is to increase daily milk production in adult cows by use of a dietary supplement of proteins derived from colostrum. The method of accomplishing these and other objectives will become apparent from the following description of the invention.

SUMMARY OF THE INVENTION

The invention relates to use of colostrum to prepare a protein rich whey product which has a number of uses. The invention relates to a method of stimulating growth in calves by addition of a dietary supplement of dried colostrum derived proteins in particular amounts. It relates to a method of stimulating milk production in dairy cows by again administering the product as a dried diet supplement. Further the invention contemplates uses of the protein rich product as a treatment of FPT, by parental administration of the product in a sterile injectable liquid form, again in specified amounts. These uses are all based on the discovery and appreciation of the protein components of colostrum both nonspecific and immunologically active.

DESCRIPTION OF THE DRAWINGS

Figure 1 is a graph demonstrating the increase in average daily milk production for cows treated with the method of the invention.

DETAILED DESCRIPTION OF THE INVENTION

As previously stated the invention comprises several uses of a purified protein product derived from colostrum. One method of collecting and purifying the bovine colostrum to concentrate levels of specific antibodies resulting from exposure to selected antigens is disclosed in Plymate, U.S. Patent No. 4,051,235. Contrary to methods such as this, the product of this invention concentrates not just IgG but all other proteins present in colostrum. Traditional thinking as exemplified by Plymate is that it is the immunoglobulins alone which are important in colostrum.

This invention acknowledges that colostrum can be valuable in parentally imparting passive immunity after gut closure but also is quite valuable for its other components. Calves treated with the colostrum derived protein whey as a dried diet supplement experienced increased weight gain over those without supplement. Also, those adults receiving the supplement had increased daily milk production compared to control and finally when administered in injectable liquid form the product increases serum immunoglobulin levels. As used herein, the term whey shall mean a purified colostrum derived product from which fat and casein have been removed comprising immunoglobulins and other proteins as earlier described, and is specifically intended to

exclude whey derived from other sources such as noncolostrum-type milk.

PREPARATION OF COLOSTRUM

First milking colostrum is procured from Grade A dairy herds located throughout different areas. Once collected, colostrum filled containers are frozen until needed. Upon production demand colostrum is thawed at ambient temperature for 8 to 24 hours and emptied into a vessel.

Casein and fat are removed from the colostrum mixture by introduction of one-half of an ounce of calcium chloride and one ounce of microbial rennet per ten gallons of colostrum.

The colostrum is agitated and the temperature is elevated to 85°F by hot water heat exchangers. Coagulation begins and the agitators are shut off. The resulting curd is cut with curd knives to allow fat to float into and through the curd. The fat is then trapped within, and on top of, the curd, resulting in a nearly fat-free whey.

The colostrum derived whey is filtered to remove microorganisms and finally passed through a cream separator to remove any remaining fat. The treated and preserved whey is then stored in a refrigerated tank at 2°C to 5°C. The whey is then filtered and reduced in volume. The resulting concentrated product is then adjusted to a pH of 6.4 to 6.6 by the addition of 2% sodium hydroxide or any other acceptable method. The protein content is diluted to 6-7% by the addition of physiological saline solution. The whey is then filter sterilized for administration to calves. The resulting whey, which contains immunoglobulins and nonspecific

proteins, is safely injectable, and its effectiveness is not dependent on oral administration and absorption across the gut during the relatively short "window of opportunity".

The whey is eventually placed in 120 ml serum bottles and stored in a cooler at 37°F plus or minus 3°F. Afflicted calves are then treated with the sterile whey product. Calves under 1-21 days old are given the product either orally or subcutaneously in a dosage of 5 ml per pound of body weight. Calves 3 to 7 days of age are given 5 ml per pound of body weight subcutaneously or intravenously. Animals subjected to this treatment experienced an increase in immunoglobulin concentration as illustrated by the following examples. Optionally the product may be spray dried into a powder form for dietary feed supplementation. Further, unexpectedly, when the same product is included in the diet of calves or adult cows in amounts of 1/10 to 2/5 oz. per day per animal, the presence of nonspecific and other essential proteins promoted growth, stimulated milk production, and improved the overall health of the animals. It should be noted that amounts are not critical and since the product is all natural virtually any practical amount within the range of economic limits can be administered.

EXAMPLE 1
Effects on Milk Production

A study was conducted in a producing dairy herd at Van Vliet Dairy Farm, Escalon, California over a period of approximately forty (40) weeks. Only first and second calf heifers were included with an average of approximately 440 animals being evaluated

on a daily basis for a total of 650 heifers being used in the entire study. Animals in the study had all been properly vaccinated for all appropriate pathogens and in addition producing cows were routinely monitored on a Dairy Herd Improvement (DHI) program for at least two months prior to entering this study and throughout the test period. The cows were all housed in identical fashion and fed the same base rations (standardized Total Mixed Rations(TMR)) throughout the study. Milk production was monitored daily for individual cows. Any cow evidencing a somatic cell count higher than 350,000 was continued on the appropriate regime, but its daily milk production was excluded from the study records. Following standard treatments utilized on the dairy farm and lowering the count below 200,000 the cows daily production was again entered into the study records.

The cows were divided into two major groups, first calf heifers and second calf heifers. Major groups were further divided as follows:

Group A - second calf heifers which received spray dried powdered form of the invention during the first eighteen (18) weeks of the study, were allowed to lapse for two weeks, and remained untreated for the last eighteen (18) weeks of the study.

Group B - second calf heifers which remained untreated during the first eighteen (18) weeks of the study, were allowed to lapse for two weeks, and then received product of the invention for the last eighteen (18) weeks of the study.

Group C - first calf heifers which received product of the invention during the first eighteen

(18) weeks of the study, were allowed to lapse for two weeks, and remained untreated for the last eighteen (18) weeks of the study.

Group D - first calf heifers which remained untreated during the first eighteen (18) weeks of the study, were allowed to lapse for two weeks, and then received product of the invention for the last eighteen (18) weeks of the study.

The product of the invention in a dried form was mechanically blended into the bulk standardized Total Mixed Ration on a daily basis. A fixed quantity of ration either with or without the product was fed to each cow daily. During the first 10 days of treatment each animal received a daily dose of 0.4 ounce of the product in its ration. On all subsequent days the dose was equal to 0.2 ounce of the product.

The daily average milk production in each group was calculated based upon the daily output during each week of the study. In all cases, the eighteen (18) week treatment period values were compared with the same group's own values obtained during the eighteen (18) week period when no treatment was given. Upon analysis of the results, it was shown that administration of the product in the diet of first and second calf heifers provided an effective means to increase milk production. There appeared to be no difference in response in terms of increased production in either first or second calf heifers. Overall increase in average daily milk production was 8% during the entire eighteen (18) treatment weeks of the study for all groups evaluated in comparison to the untreated period for the same groups. Secondary analysis of the data

indicated that the primary effect of the product in this study occurred during the first 10 weeks after treatment commenced and then slowly diminished. Comparatively the average daily milk production was improved by more than 11% for all groups studied during this period. In contrast a combined change of only 4% was observed during the last eight weeks of treatment period. This differential was seen in both the first and second calf heifers

Figure 1 is a graph demonstrating the increase in average daily milk production for cows treated with the method of the invention.

It is submitted that the unexpected improvement in milk production is a surprising result as colostrum has been characteristically considered only as a source of immunoglobulins. It is clear that there are other proteins in the preparation which have significant effects on overall cow health and productivity. These results could not be simply due to the presence of immunoglobulins in the product as administration occurred after gut closure, indicating the value of the other components in the purified colostrum product.

While not wishing to be bound by any theory, it is submitted that the nonspecific proteins present in the colostrum preparation of the invention contain hormone precursors which may act to stimulate milk production. Applicant is clearly the first to appreciate the benefits of these additional proteins as most supplements are designed to isolate purely immunoglobulins. As in Scott, U.S. Patent number 4,834,974 which prepares an immunoglobulin product from liquid by-product from cheese

preparation or regular casein removed milk, not colostrum.

Tables 1-4 indicate the specific results obtained on treatment with the method of the invention in the various subgroups.

SUMMARY OF EFFECT OF TREATMENT WITH DRIED, PURIFIED COLOSTRUM ON AVERAGE DAILY MILK PRODUCTION (LBS.) IN SECOND CALF HEIFERS GROUP A

	DURING TREATMENT			UNTREATED		
Week	No. Days Monitored	Avg. No. Cows	Avg. Daily Production	No. Days Monitored	Avg. No. Cows	Avg. Daily Production
1	7	84	87.8	6	77	79.5
2	6	84	88.5	7	75	79.4
3	7	82	90.8	6	74	77.6
4	6	80	91.4	7	74	79.0
5	7	81	89.2	6	72	80.9
6	7	87	82.5	7	70	81.1
7	7	90	82.8	5	69	78.3
8	6	90	87.9	7	67	78.4
9	7	87	89.7	6	67	75.0
10	6	93	87.0	7	69	73.7
11	6	96	87.2	7	72	74.1
12	6	95	85.4	6	74	73.5
13	7	92	85.5	6	75	72.6
14	6	89	86.0	6	79	74.5
15	7	87	83.1	7	76	77.2
16	6	83	83.7	4	69	79.5
17	7	82	82.8	7	70	80.1
18	7	80	81.6	6	71	79.8
Mean	6.6	86.8	86.3	6.2	72.2	77.5
Change	–	–	+11.4%	–	–	–
Mean (wk. 1–10)	6.6	85.8	87.8	6.4	71.4	78.3
Change	–	–	+12.1%	–	–	–
Mean (wk. 11–18)	6.5	88.0	84.4	6.0	73.3	76.4
Change	–	–	+10.5%	–	–	–

SUMMARY OF EFFECT OF TREATMENT WITH DRIED, PURIFIED COLOSTRUM ON AVERAGE DAILY MILK PRODUCTION (LBS.) IN SECOND CALF HEIFERS GROUP B

	DURING TREATMENT			UNTREATED		
Week	No. Days Monitored	Avg. No. Cows	Avg. Daily Production	No. Days Monitored	Avg. No. Cows	Avg. Daily Production
1	6	116	83.1	7	79	80.0
2	7	115	84.6	6	83	78.5
3	6	118	84.0	7	83	80.8
4	7	119	87.1	6	87	80.0
5	6	112	91.2	7	90	80.8
6	7	112	92.0	7	86	79.6
7	5	112	90.5	7	85	79.2
8	7	116	92.2	6	89	81.4
9	6	116	89.5	7	92	82.0
10	7	114	88.6	6	93	81.9
11	7	111	88.0	6	94	82.0
12	6	110	84.2	6	102	80.3
13	6	109	81.7	6	106	79.6
14	5	109	82.0	7	107	81.4
15	7	107	82.7	6	107	81.9
16	4	106	83.5	7	108	81.0
17	7	108	83.0	7	116	82.1
18	6	111	81.5	7	114	83.2
Mean	6.2	112.3	86.1	6.6	95.6	80.9
Change	–	–	+6.4%	–	–	–
Mean (wk. 1–10)	6.4	115.0	88.3	6.6	86.7	80.4
Change	–	–	+9.8%	–	–	–
Mean (wk. 11–18)	6.0	108.9	83.3	6.5	106.6	81.4
Change	–	–	+2.3%	–	–	–

SUMMARY OF EFFECT OF TREATMENT WITH DRIED, PURIFIED COLOSTRUM ON AVERAGE DAILY MILK PRODUCTION (LBS.) IN FIRST CALF HEIFERS GROUP C

	DURING TREATMENT			UNTREATED		
Week	No. Days Monitored	Avg. No. Cows	Avg. Daily Production	No. Days Monitored	Avg. No. Cows	Avg. Daily Production
1	7	125	77.6	6	131	67.3
2	6	123	77.5	7	130	66.7
3	7	120	79.0	6	129	66.2
4	6	119	78.6	7	131	67.9
5	7	118	77.7	6	125	70.6
6	7	118	71.3	7	125	70.4
7	7	117	72.4	5	126	68.5
8	6	116	76.7	7	125	70.1
9	7	116	77.0	6	118	69.0
10	6	115	74.9	7	121	68.7
11	6	125	73.7	7	123	67.8
12	6	137	71.0	6	126	66.3
13	7	140	71.7	6	123	65.6
14	6	139	72.2	5	118	66.4
15	7	139	68.1	7	120	67.2
16	6	138	68.6	4	117	68.5
17	7	135	69.0	7	114	70.3
18	7	132	68.7	6	113	72.3
Mean	6.6	126.2	73.7	6.2	123.1	68.3
Change	–	–	+7.9%	–	–	–
Mean (wk. 1–10)	6.6	118.7	76.3	6.4	126.1	68.5
Change	–	–	+11.4%	–	–	–
Mean (wk. 11–18)	6.5	135.6	70.4	6.0	119.3	68.1
Change	–	–	+3.4%	–	–	–

SUMMARY OF EFFECT OF TREATMENT WITH DRIED, PURIFIED COLOSTRUM ON AVERAGE DAILY MILK PRODUCTION (LBS.) IN FIRST CALF HEIFERS GROUP D

	DURING TREATMENT			UNTREATED		
Week	No. Days Monitored	Avg. No. Cows	Avg. Daily Production	No. Days Monitored	Avg. No. Cows	Avg. Daily Production
1	6	144	70.7	7	109	64.9
2	7	140	72.5	6	112	64.7
3	6	137	72.7	7	114	65.1
4	7	135	74.9	6	121	65.1
5	6	133	76.5	7	121	66.9
6	7	132	76.2	7	126	64.0
7	5	132	74.5	7	128	65.6
8	7	131	75.1	6	129	69.1
9	6	129	74.0	7	128	69.8
10	7	128	73.2	6	132	70.4
11	7	127	72.2	6	138	70.8
12	6	126	71.3	6	137	70.6
13	6	125	71.6	7	138	70.3
14	5	124	70.4	6	138	71.1
15	7	128	70.6	7	141	69.9
16	4	128	71.1	6	140	70.6
17	7	132	68.4	7	142	71.3
18	6	132	67.7	7	143	71.5
Mean	6.2	130.9	72.4	6.6	129.8	68.4
Change	–	–	+5.8%	–	–	–
Mean (wk. 1–10)	6.4	134.1	74.0	6.6	122.0	66.6
Change	–	–	+11.1%	–	–	–
Mean (wk. 11–18)	6.0	126.9	70.4	6.5	139.6	70.8
Change	–	–	−0.6%	–	–	–

EXAMPLE 2

A growing barn supplemented the diet of 135 calves with 1/10th ounce per calf daily of VP-127, the product of the invention containing premium quality dried colostral powder, for a total of 138 consecutive days. An equal number of calves were fed the same diet without VP-127. This is what they reported.

	Fed VP-127	Not Fed VP-127
Weight In (Lbs.)	83.00	83.00
Weight Out - Live	417.79	402.44
Dressed Weight	280.84	270.36

That meant an average increase of 15.35 pounds in live weight and 10.48 in dressed weight for the calves fed VP-127. A total of 118 animals were dressed-out in the supplemented group and represented more than 1,235 extra pounds. And they found that the calves were healthier and required less medication, further reducing costs and increasing profits.

EXAMPLE 3

Efficacy Studies of Calves Treated Subcutaneously With Sterile Purified Colostrum (ID-1) at 3-6 Days of Age

Calves. Twenty bull calves were used in this example. The calves were fed milk replacement for nutritional support and received no supplemental colostrum. Blood samples were collected and were

used to determine starting serum immunoglobulin concentration by radial immunodiffusion assay (RID).

Calves defined as having FPT were those with a serum immunoglobulin (IgG) concentration of less than 800 mg/dl and those with partial FPT with serum immunoglobulin (IgG) concentrations of 800 to 1600 mg/dL, with over 1600 mg/dL as normal (adapted from McGuire, T.C. and D.S. Adams, 1982). Because the herd had fewer calves than anticipated, some calves that were selected for the study had higher serum IgG concentration than a defined FPT level. Calves were assigned to control and treatment groups randomly and weight was determined using a dairy cattle and calf weight measuring tape.

Treatment. Calves assigned to the treatment group were injected subcutaneously with 400 ml of the product of the invention in liquid injectable form (trade name ID-1). The ID-1 contained 6.0% protein, 72% of which was immunoglobulin (IgG) (as determined by agarose gel electrophoresis). This is equivalent to 4.32 g of immunoglobulin per 100 ml of ID-1. Thus, a 100 pound calf would receive the following:

400 ml ID-1 = 17.28 g immunoglobulin (4 x 4.32 g/100 ml)

30 ml plasma/pound x 100 pounds = 3000 ml plasma

17.28 g/3000 ml = 5.8 g of immunoglobulin (if 100% absorbed)

Sample collection. Blood samples were collected prior to, and 24 and 48 hours after ID-1 treatment. Immunoglobulin (IgG) levels in these blood samples, as determined by radial immunodiffusion (RID), were used to demonstrate the efficacy of ID-1 in

increasing serum immunoglobulin levels in calves older than 24 hours of age.

Determination of blood immunoglobulin levels. Blood immunoglobulin (IgG) concentrations were determined by radial immunodiffusion (RID), with antisera specific for bovine IgG. The precipitin rings formed in the sample wells were compared to those for bovine IgG standards supplied by the manufacturer of the kit (VMRD, Pullman, WA). The ring diameters for sample and standards were entered into a computer program that then calculated the predicted concentration of immunoglobulins (IgG) in the serum.

Calculation of percent of IgG absorbed. The percent of IgG absorbed was calculated by comparison of the RID data from pre- and post-treatment samples. Knowing the dose of immunoglobulin given, the maximum amount of immunoglobulin that could have been absorbed, if there was 100% absorption, was calculated. From this value, and knowing the amount of IgG given, the actual percent absorption was calculated.

Results. All calves were observed to be typical "Grade B" calves. They were strong and ate the first feeding well. The next morning, all calves were sick and required much supportive therapy; all calves were treated with antibiotics, protein, and typical veal calf supportive therapy. Four of the calves in the control group died by the second day. The ID-1 treated calves seemed to respond well to the treatment, and no treated calves died. The

serum immunoglobulin concentrations at 0, 24, and 48 hours are presented in Table 5.

The mean relative change at 48 hours was:

control (FPT; shaded; N=1) - 31%; control (non-FPT; N=5) -16.6%
treated (FPT; shaded; N=7) 57.9%; treated (non-FPT; N=3) 1%

The amount of immunoglobulin absorbed (as determined by RID, and as a calculated percentage is presented in Table 6.

The mean relative percent absorbed (calculated) was:

control (FPT; shaded; N=1) -31.2%; control (non-FPT; n=5 -23.3%
treated (FPT; shaded; N=7) 79.3%; treated (non-FPT; n=3) 6.6%

From Table 6, column heading "IgG absorbed (mg/dL)", the mean absolute change in immunoglobulin concentration at 48 hours may be discerned:

control (FPT; shaded; N=1 -451p control (non-FPT; N=5) 9413
treated (FPT; shaded; N=7) 334.7; treated (non-FPT; N=3) 2.3

Table 5 Serum immunoglobulin concentration before and after ID-1 treatment of calves 3-6 days of age. Control and treatment calves are listed in order of the pre-treatment immunoglobulin concentration.*

Serum Immunoglobulin Concentration (mg/dL)

Calf number	Group	Pre-treatment	Post treatment (24 hrs)	Post treatment (48 hrs)	Relative change (24 hrs)	Relative change (48 hrs)
21	C	1446	970	995	-33%	-31%
3	C	1743	947	1778	-46%	2%
9	C	1992	no sample	1490	no sample	-25%
18	C	2123	1879	1594	-11%	-25%
24	C	3059	584	1857	-81%	-39%
27	C	3800	1378	3933	-64%	4%
5	T	254	264	295	4%	16%
16	T	317	355	995	12%	214%
7	T	491	525	663	7%	35%
8	T	954	622	1778	-35%	86%
10	T	1029	843	1328	-18%	29%
4	T	1226	1330	1473	8%	20%
2	T	1538	1046	1620	-32%	5%
29	T	1793	3011	1957	68%	9%
28	T	2282	1948	2219	-15%	-3%
19	T	3313	2697	3219	-19%	-3%

* Note: Data that is shaded is from calves whose pre-treatment serum immunoglobulin concentrations fit the definition of complete or partial failure of passive transfer,

Table 6 Calculated percent immunoglobulin absorbed 48 hours after ID-1 treatment of calves 3-6 days of age. Note: Data that is shaded is from calves whose pre-treatment serum immunoglobulin concentrations fit the definition of complete or partial failure of passive transfer.

Calf number (T/C)*	Body Weight (by tape)	Estimated ml of plasma	IgG absorbed (mg/dL)**	% absorbed (calculated)	IgG absorbed of 100% absorbed
2(T)	96	2880	82	21	395
4(T)	96	2880	247	63	395
5(T)	85	2550	41	9.2	447
7(T)	89	2670	172	40.3	427
8(T)	89	2670	824	192.9	427
10(T)	89	2670	299	70	427
16(T)	89	2670	678	158.8	427
19(T)	96	2880	-94	-2.8	395
28(T)	86	2580	-63	-14.3	442
29(T)	86	2580	164	37	442
3(C)	96	2880	35+	2+	_++
9(C)	89	2670	-502	-25.2	-
18(C)	89	2670	-529	-25	-
21(C)	103	3090	-451	-31.2	-
24(C)	87	2610	-1238	-40.5	-
27(C)	100	3000	133	3.5	-

* T=treated with 400 ml of ID-1; C untreated control calf

** calculated from RID data, Table 2; (48 hr - 0 hr)

+ value listed for control calves indicates change from Time 0 value, as measured at 48 hours; because they were not treated with ID-1, a percent absorption cannot be calculated

++ calculation of IgG absorbed if 100% was absorbed was not performed for control calves because they were not treated with ID-1

EXAMPLE 4

Calves Treated Subcutaneously at 7 to 21 Days of Age

Calves. Twelve bull calves were used in this example. The calves were fed milk replacement for nutritional support, received no supplemental colostrum, and initial blood samples were collected and used to determine starting serum IgG concentrations (by radial immunodiffusion assay). All calves in this example had serum IgG concentrations defined as at least partial FPT. The calves were weighed, treated with the same amount of ID-1 as in Example 3, blood samples were collected in the same way as for Example 3, and determination of blood immunoglobulin levels and calculations of percent of IgG absorbed were identically performed.

Results. All calves were observed to be typical "Grade B and C" calves. They required much medication and supportive therapy; all calves were treated heavily with antibiotics. The ID-1 treated calves seemed to respond well to treatment, and no treated calves died. One control calf died. The serum immunoglobulin (IgG) concentration at 0, 24, and 48 hours is presented in Table 7. The mean relative change at 48 hours was: control (N = 5) -17.4%; treated (N = 7) 97.9% or (N = 6) 35.7%*. The amount of immunoglobulin (IgG) absorbed (as determined by RID, and as a calculated percentage) are presented in Table 8. The mean relative percent absorbed (calculated) was: control (N = 5) -22.56%; treated (N = 7) 111.6% or (N = 6) 71.1%*. From Table 8, column heading "IgG absorbed (mg/dL)", the mean absolute range of immunoglobulin concentration at 48 hours may be discerned: control (N = 5)

-154%; treated (N = 7) 518.4% or (N = 6) 282.8%*. (if number 207 is not included in calculation; its change at 48 hours was 471%).

Table 7 Serum immunoglobulin concentration before and after ID-1 treatment of calves 7-21 days of age. Control and treatment calves are listed in order of the pre-treatment immunoglobulin concentration.

Serum Immunoglobulin Concentration (mg/dL)

Calf number	Group	Pre-treatment	Post treatment (24 hrs)	Post treatment (48 hrs)	Relative change (24 hrs)	Relative change (48 hrs)
175	C	321	276	364	-14%	13%
185	C	354	396	177	12%	-50%
208	C	432	423	408	-2%	-6%
215	C	1151	1436	728	25%	-37%
206	C	1431	2039	1329	42%	-7%
204	T	233	356	341	53%	46%
207	T	410	1399	2342	241%	471%
188	T	542	507	646	-6%	19%
192	T	866	982	1261	13%	46%
198	T	1024	1563	1471	53%	44%
214	T	1091	1634	1699	50%	56%
210	T	1215	1531	1250	26%	3%

Table 8 Calculated percent immunoglobulin absorbed 48 hours after ID-1 treatment of calves 7-21 days of age.

Calf number (T/C)*	Body Weight (by tape)	Estimated ml of plasma	IgG absorbed (mg/dL)**	% absorbed (calculated)	IgG absorbed if 100% absorbed
188(T)	96	2880	104	22	476
192(T)	103	3090	395	81	443
198(T)	103	3090	447	99	443
204(T)	94	2820	108	22	489
207(T)	84	2520	1932	355	544
210(T)	110	3300	35	8.4	415
214(T)	146	4380	608	194	313
185(C)	114	3420	-177+	-50+	-++
206(C)	84	2520	-104	-7	-
208(C)	89	2670	-24	-5.6	-
175(C)	85	2550	-42	-13.4	-
215(C)	122	3660	-423	-36.8	-

*=treated with 480 ml of ID-1; c=untreated control calf

**calculated from RID data, Table 7; (48 hr - 0 hr)

+value listed for control calves indicates change from Time 0 value, as measured at 48 hours; because they were not treated with ID-1, a percent absorption cannot be calculated

++calculation of IgG absorbed if 100% was absorbed was not performed for control calves because they were not treated with ID-1

EXAMPLE 5
Calves Treated Subcutaneously or Intravenously at 3 - 7 Days of Age

Calves. Thirty-nine bull calves were used in this example. The calves were fed milk replacement for nutritional support. The calves did not receive any supplemental colostrum. Blood samples were collected from calves and were used to determine the

baseline serum IgG concentration (by radial immunodiffusion assay; RID). Because the baseline IgG concentration cannot be predicted before it is actually measured, some calves had higher serum IgG concentrations than the defined FPT level. Calves were assigned to control and treatment groups randomly, at the time of the first bleeding. Weight was determined using a Dairy Cattle and Calf Weight Measuring Tape. The 12 calves assigned to the control group were untreated.

Subcutaneous Treatment. The 19 calves assigned to the subcutaneous treatment group were injected with 400 ml of ID-1. The ID-1 contained 6.0% protein, 72% of which was immunoglobulin (IgG) as determined by agarose gel electrophoresis. This is equivalent to 4.32 g of immunoglobulin (IgG) per 100 ml of ID-1.

Intravenous Treatment. The eight (8) calves assigned to the intravenous treatment group were injected with 240 ml of ID-1. The ID-1 contained the same amount of protein and immunoglobulin as described above, and is equivalent to 4.32 g of immunoglobulin (IgG) per 100 ml of ID-1.

Sample collection. Blood samples were collected prior to, and 24 and 48 hours after ID-1 treatment. Immunoglobulin (IgG) levels in these blood samples, as determined by RID, were used to demonstrate the efficacy of ID-1 in increasing serum immunoglobulin (IgG) levels in calves 3 - 7 days of age as described earlier.

RESULTS

All calves were observed to be typical "Grade B" calves. Many calves appeared sickly and had what appeared to be nutritional diarrhea, but supportive therapy was delayed until after the 48-hour blood sample was collected. Two of the calves, one in the control group and one in the IV treatment group died before the 24 hour blood sample could be taken.

The serum immunoglobulin (IgG) concentrations at 0, 24, and 48 hours are presented in Tables 9 and 10. The mean relative change at 24 and 48 hours was:

Mean relative change at 24 hours:

control (FPT; shaded; N=5) 42.8%; control (non-FPT; N=6) -4.3%
IV treated (FPT; shaded; N=4) 95.8%; IV treated (non-FPT; N=3) 25.3%
SQ treated (FPT; shaded; N=8) 85.5%; SQ treated (non-FPT; N=11) 23.9%

Mean relative change at 48 hours:

control (FPT; shaded; N=5) 32.8%; control (non-FPT; N=6) -8.8%
IV treated (FPT; shaded; N=4) 84.3%; IV treated (non-FPT; N=3) 45.3%
SQ treated (FPT; shaded; N=8) 116.1%; SQ treated (non-FPT; N=11) 7.4%

The amount of immunoglobulin (IgG) absorbed (as determined by RID, and as calculated percentage) are presented in Tables 11 and 12. The mean relative percent absorbed (calculated) was:

Mean relative % absorbed at 24 hours:

control (FPT; shaded; N=5) 14.0%; control (non-FPT; N=6) -6.3%
IV treated (FPT; shaded; N=4) 83.5%; IV treated (non-FPT; N=3) 216.7%
SQ treated (FPT; shaded; N=8) 50.1%; SQ treated (non-FPT; N=11) 166.8%

Mean relative % absorbed at 48 hours:

control (FPT; shaded; N=5) 13.6%; control (non-FPT; N=6) -7.0%
IV treated (FPT; shaded; N=4) 77.5%; IV treated (non-FPT; N=3) 473.7%
SQ treated (FPT; shaded; N=8) 92.6%; SQ treated (non-FPT; N=11) 36.4%

From Tables 11 & 12, column headings "IgG observed (mg/dL)" and "IgG absorbed (mg/dL)", the mean absolute change in immunoglobulin concentration at 24 and 48 hours may be discerned:

Mean absolute change at 24 hours:

control (FPT; shaded; N=5) 35.0%; control (non-FPT; N=6) -19.3%
IV treated (FPT; shaded; N=4) 214.5%; IV treated (non-FPT; N=3) 512.7%
SQ treated (FPT; shaded; N=8) 209.8%; SQ treated (non-FPT; N=11) 687.2%

Mean absolute change at 24 hours:

control (FPT; shaded; N=5) -23.6%; control (non-FPT; N=6) 295.7%
IV treated (FPT; shaded; N=4) 195.5%; IV treated (non-FPT; N=3) 1145.7%
SQ treated (FPT; shaded; N=8) 370.8%; SQ treated (non-FPT; N=11) 156.1%

Table 9 Serum immunoglobulin concentration before and after ID-1 treatment of calves 3-7 days of age. Control and IV treatment calves are listed in order of the pre-treatment immunoglobulin concentration.*

Serum Immunoglobulin Concentration (mg/dL)

Calf number	Group	Pre-treatment	Post treatment (24 hrs)	Post treatment (48 hrs)	Relative change (24 hrs)	Relative change (48 hrs)
1486	C	37	114	87	208%	135%
1465	C	181	168	211	-7%	17%
1458	C	268	298	390	11%	46%
1469	C	704	647	556	-8%	-21%
1574	C	1327	1465	1155	10%	-13%
1480	C	2412	2236	1894	-7%	-21%
1491	C	2571	1879	1193	-27%	-54%
1483	C	3310	3149	9260	-5%	180%
1577	C	3314	3244	2981	-2%	-10%
1569	C	4629	4826	2622	4%	-43%
1475	C	7213	7999	7273	11%	1%
1468	IV	116	238	125	105%	8%
1575	IV	163	315	423	93%	160%
1457	IV	254	476	476	87%	87%
1655	IV	354	716	645	102%	82%
1559	IV	1696	2348	2303	38%	36%
1653	IV	2371	3300	4280	39%	81%
1489	IV	4799	4756	5720	-1%	19%

*Note: Data that is shaded is from calves whose pre-treatment serum immunoglobulin concentrations fit the definition of complete or partial failure of passive transfer.

Table 10 Serum immunoglobulin concentration before and after ID-1 treatment of calves 3-7 days of age. Subcutaneous treatment calves are listed in order of the pre-treatment Immunoglobulin concentration.*

		Serum Immunoglobulin Concentration (mg/dL)				
Calf number	Group	Pre-treatment	Post treatment (24 hrs)	Post treatment (48 hrs)	Relative change (24 hrs)	Relative change (48 hrs)
1485	SQ	87	298	244	243%	180%
1461	SQ	98	208	231	112%	136%
1459	SQ	163	298	613	83%	276%
1566	SQ	209	526	591	152%	183%
1481	SQ	510	715	678	40%	33%
1487	SQ	1172	1384	1193	18%	2%
1479	SQ	1340	1733	1644	29%	23%
1463	SQ	1408	1503	2759	7%	96%
1576	SQ	1756	3065	2048	75%	17%
1466	SQ	1826	2182	2170	19%	19%
1573	SQ	2584	3846	3400	49%	32%
1565	SQ	2909	2865	2934	-2%	1%
1472	SQ	2910	3664	3145	26%	8%
1490	SQ	3109	2946	3442	-5%	11%
1570	SQ	3468	3634	3400	5%	-2%
1482	SQ	3524	2939	4135	-17%	17%
1484	SQ	3750	4433	3786	18%	1%
1578	SQ	3953	3765	2463	-5%	-38%
1478	SQ	3990	7999	4573	100%	15%

*Note: Data that is shaded is from calves whose pre-treatment serum immunoglobulin concentrations fit the definition of complete or partial failure of passive transfer.

Table 11 Calculated percent immunoglobulin (IgG) present in blood 24 and 48 hours after ID-1 treatment of calves 3-7 days of age. Data for control and IV treatment calves is listed in order of ear tag number. Note: Data that is shaded is from calves whose pre-treatment serum immunoglobulin concentrations fit the definition of complete or partial failure of passive transfer.

Calf number/ group*	Body weight	Estimated ml of plasma	IgG available if 100% present	IgG observed (mg/dl) (24 hrs)**	% present (calculated (24 hrs)	IgG observed (mg/dl) (48 hrs)**	% present (calculated) (48 hrs)
1458/C	85	2550	-	30	10%	122	41%
1465/C	89	2670	-	-13	-8%	30	10%
1469/C	82	2460	-	-57	-9%	-148	-23%
1475/C	89	2670	-	786	10%	60	1%
1480/C	94	2820	-	-176	-8%	-518	-23%
1483/C	85	2550	-	-161	-5%	5950	189%
1486/C	103	3090	-	77	68%	50	44%
1491/C	85	1550	-	-692	-37%	-1378	-73%
1569/C	89	2670	-	197	4%	-2007	-42%
1574/C	89	2670	-	138	9%	-172	-12%
1577/C	94	2820	-	-70	-2%	-333	-10%
1457/IV	82	2460	278	222	80%	222	80%
1468/IV	89	2670	256	122	48%	9	4%
1489/IV	82	2460	278	-43	-15%	921	331%
1559/IV	86	2570	266	652	245%	607	228%
1575/IV	98	2940	233	152	65%	260	112%
1653/IV	103	3090	221	929	420%	1909	862%
1655/IV	89	2670	256	362	141%	291	114%

*IV=treated intravenously with 240 ml of ID-1; C=untreated control calf

**calculated from RID data, Table 9; (24 hr - 0 hr; 48 hr - 0 hr)

Table 12 Calculated percent immunoglobulin (IgG) absorbed 24 and 48 hours after ID-1 treatment of calves 3-7 days of age. Data for SQ treatment calves is listed in order of ear tag number. Note: Data that is shaded is from calves whose pre-treatment serum immunoglobulin concentrations fit the definition of complete or partial failure of passive transfer.

Calf number/ group*	Body weight	Estimated ml of plasma	IgG absorbed if 100% absorbed	IgG absorbed (mg/dL) (24 hrs)**	% absorbed (calculated (24 hrs)	IgG absorbed (mg/dL) (48 hrs)**	% absorbed (calculated) (48 hrs)
1459/SQ	82	2460	463	135	29%	450	97%
1461/SQ	89	2670	427	110	26%	133	31%
1463/SQ	103	3090	369	95	26%	1351	366%
1466/SQ	89	2670	427	356	83%	344	81%
1472/SQ	84	2520	452	754	167%	235	52%
1478/SQ	87	2610	437	4009	918%	583	133%
1479/SQ	91	2730	418	393	94%	304	73%
1481/SQ	85	2550	447	205	46%	168	38%
1482/SQ	83	2490	458	-585	-128%	611	133%
1484/SQ	94	2820	404	683	169%	36	9%
1485/SQ	82	2460	463	211	46%	157	34%
1487/SQ	96	2880	396	212	54%	21	5%
1490/SQ	89	2670	427	-163	-38%	333	78%
1565/SQ	96	2880	396	-44	-11%	25	6%
1566/SQ	96	2880	396	317	80%	382	97%
1570/SQ	96	2880	396	166	42%	-68	-17%
1573/SQ	100	3000	380	1262	322%	816	215%
1576/SQ	89	2670	427	1309	307%	292	68%
1578/SQ	91	2730	418	-188	-45%	-1490	-357%

*SQ=treated subcutaneously with 400 ml of ID-1; C=untreated control calf

**calculated from RID data, Table 10; (24 hr - 0 hr; 48 hr - 0 hr)

What is claimed is:

1. A product for treating failure of passive transfer and supplementing the diet of cows comprising: a preparation of proteins purified from bovine colostrum; said preparation including immunoglobulins and nonspecific proteins.

2. The product of claim 1 wherein said preparation is colostrum from which fat and casein have been removed.

3. The preparation of claim 1 wherein said proteins include: transferrin, lactoferin, lysozyme, xanthine oxidase, lactoperoxidase, insulin-like growth promoting factors, conglutinin, β-lysin and ubiquitin.

4. A method of treatment for failure of passive immunity transfer (FPT) in calves, said method comprising: collecting colostrum from dairy cows; removing casein and fat from said colostrum to prepare a serum of immunoglobulins and nonspecific proteins present in said colostrum; sterilizing said serum; and administering said serum to a calf.

5. The method of claim 4 wherein said bovine colostrum serum contains immunoglobulins and nonspecific proteins.

6. The method of claim 5 wherein said nonspecific proteins impart increase cellular immunity and stimulate cellular activity.

7. The method of claim 4 wherein said serum is injected into a calf.

8. The method of claim 4 wherein said blood immunoglobulin and nonspecific protein concentration is increased in calves over 24 hours old.

9. The method of claim 4 wherein said serum results in blood immunoglobulin levels of at least one-fourth that of a normal calf that has received passive immunity within 24 hours after administration.

10. The method of claim 4 wherein 70% to 80% of subcutaneously injected immunoglobulin is absorbed.

11. A method of treatment for failure of passive immunity transfer in calves, said method comprising: collecting bovine colostrum; removing casein and fat from said collected colostrum, to prepare a serum from remaining immunoglobulins and nonspecific proteins present in said colostrum; sterilizing said serum for injection, and injecting an effective amount of said serum intravenously into an affected calf, said calf being at an age where its gut has essentially closed.

12. The method of claim 11 wherein 100% of immunoglobulin administered is immediately utilized by the affected calf.

13. The method of claim 11 wherein the affected calf exhibits no swelling or discomfort from injection.

14. The method of claim 11 wherein said bovine colostrum contains immunoglobulins and nonspecific proteins.

15. The method of claim 14 wherein said nonspecific proteins impart increased cellular immunity to affected calves.

16. The method of claim 11 wherein said calf is from 24 hours to 21 days old.

17. The method of claim 11 wherein said serum is a colostrum replacement.

18. A method of preparing a product for treatment of FPT and for improving health of cows comprising: collecting colostrum from dairy cows; removing casein and fat from said colostrum to prepare a serum of immunoglobulins and nonspecific proteins present in said colostrum; sterilizing said serum; and administering said serum to a cow.

19. The method of claim 18 further comprising the step of drying said serum to form a powder.

20. A product useful for treating FPT comprising: a sterile purified colostrum product from which fat and casein have been removed.

21. The product of claim 20 comprising immunoglobulins and nonspecific proteins

22. A method of improving milk production and growth rates in adult and young cows comprising: supplementing the diet of said cows with a purified protein serum derived from bovine colostrum.

23. The method of claim 22 wherein said supplementation is 1/10 - 2/5 oz. of product per cow per day.

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Databases (see below)
(i) UK Patent Office collections of GB, EP, WO and US patent specifications.

(ii) ONLINE: WPI, CLAIMS

Documents considered relevant following a search in respect of Claims :-
18 TO 23

Categories of documents

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Category	Identity of document and relevant passages		Relevant to claim(s)
X	EP 0391416 A1	(CHUGAI SEIYAKU KABUSHIKI KAISHA) - whole document	20, 22, 23
X	WO 81/00342 A1	(O.R.A.A (S.A.R.L) - whole document	20, 22, 23
X	WO 89/10139 A1	(BIOTEST PHARMA GMBH) - whole document	20, 22, 23
X	US 4051235	(ROBERT R PLYMATE) - whole document	20, 22, 23
X	US 4644056	(BIOTEST PHARMA GMBH) - whole document	20, 22, 23
X	JP 040275300 A	(SNOW BRAND MILK PRODUCT CO LTD) - Derwent WPI Abstract Accession No 92-376306/46	20, 22, 23

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